REMARKS

Status of the Claims

Claims 1-19 and 28 are pending in the present application, Claims 20-27 having been canceled herein as being directed to a non-elected invention (subject to applicants' right to file a divisional application during the pendency of the present application), and new Claim 28 having been added. Claims 1, 7, 13, 15, 18 and 19 have been amended to more clearly defined the invention.

Amendment of the Specification

Applicants have amended the specification in two different manners. First, inadvertent errors dealing with grammar and the title of a patent application identified by its U.S. serial number have been corrected. Second, material from a commonly assigned and co-pending U.S. patent application, which was specifically incorporated by reference in the application as filed, has been added to the specification. Neither amendment represents the addition of any new matter.

The material which had been incorporated by reference has been added to provide additional written description related to a specific type of reactor. As discussed in detail below, applicants have amended the independent claims to further define the type of reactor employed in the present invention. As amended, the claims now define an apparatus comprising a reactor configured to be operated continuously, such that a volume of product produced by the reactor is a function of the flow rate of the reactants introduced into the reactor, and a length of time during which such reactants are introduced into the reactor. Significantly, it should be recognized that the flow rate of reactants into a batch reactor is largely irrelevant, as once introduced into the reactor the reactants are held for whatever period of time is required to complete the batch process. In contrast, controlling the flow rate of reactants into a continuous process reactor is critical in enabling control of reaction times to be achieved. For example, reactions requiring relatively little reaction times can be implemented using a relatively higher flow rate, while reactions requiring relatively longer reaction times must be implemented using relatively slower flow rates.

As originally filed, the application provides a written description of a continuous flow reactor (a type of reactor which is distinguishable over a batch reactor) in the following sections: The paragraph beginning on line 16 of page 4 (which discloses using a pump to achieve a desired flow rate through the reactor), the first paragraph of page 11 (which discusses the importance of flow rates), the second complete paragraph of page 12 (which again discusses the importance of flow rates), the last paragraph on

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page 14 (which discusses flow rates and how a residence time chamber can be used to extend the reaction time), the first full paragraph of page 17 (which describes the continuous flow of reactants and solvent through the reactor), the second full paragraph of page 19 (which describes the continuous flow of reactants and solvent through the reactor in the context of FIGURE 4), and the final paragraph on page 28 (which discloses using relatively fast flow rates for reactions requiring relatively short reaction times, and using relatively slow flow rates for reactions requiring relatively long reaction times).

The previously incorporated by reference material which has been added to the specification by the present amendment provides additional written description of a preferred stack plate reactor configured for continuous operation (as opposed to batch operation). Significantly, the added material provides a detailed description of the movement of reactants and product through the preferred stack plate reactor, illustrating the continuous flow of material through the preferred reactor.

Claims Rejected under 35 U.S.C § 112, Second Paragraph

The Examiner has rejected Claims 7, 8, and 19 under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Specifically, the Examiner asserts that the phrase "heat exchanger being coupled in fluid communication with the reaction module" is unclear, because the exchangers transfer energy from one fluid to another fluid without mixing the two.

Applicants have amended Claims 7 and 19; thereby obviating the indefiniteness rejection. Accordingly, the rejection of Claims 7, 8, and 19 under 35 U.S.C § 112, second paragraph, should be withdrawn.

Claims Rejected under 35 U.S.C § 103

The Examiner has rejected Claims 1-6, 9, 11-16, and 18 under 35 U.S.C § 103(a) as being obvious over Rosenberg (WO009300625). The Examiner admits that Rosenberg does not teach each element recited in applicants' claims, but asserts that it would have been obvious to one of ordinary skill in the art to modify Rosenberg's apparatus to achieve an equivalent invention. Applicants respectfully disagree for the following reasons

Referring to Claim 1, applicants have amended Claim 1 to further define the reactor. As amended, the reactor defined in Claim 1 is configured to *operate continuously over a period of time, such that a volume of a desired product produced by the reactor is a function of both a flow rate associated with the plurality of reactants introduced into the reactor, and a length of time during which the plurality*

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of reactants are continuously introduced into the general purpose reactor, as opposed to a volume of a reactor operating in a batch mode.

The reactor disclosed by Rosenberg is specifically configured to operate in a batch mode, and there is no evidence to conclude that it would have been obvious to one of ordinary skill in the art at the time of the invention to replace the batch reactor disclosed by Rosenberg with a continuous reactor as recited in Claim 1. Significantly, there is no evidence that an artisan of ordinary skill would have recognized any benefit that could be achieved by making such a substitution, nor is it evident that such a substitution would solve any problem that had been recognized by the art.

Applicants believe that prior art sequential reaction systems have heretofore been implemented using batch reaction vessels, as opposed to a reactor configured for continuous operation. In a batch process, specific volumes of reactants are introduced into a finite reaction volume. If the reaction volume is 50 milliliters, then only 50 milliliters of product can be produced per batch (i.e., before the reactor is emptied, cleaned for reuse, and additional reactants are introduced). In contrast, a reactor configured for continuous operation will continuously receive reactants and discharge a product, such that the volume of product produced is a function of the flow rate of the reactants introduced into the reactor, and a length of time that reactant flow rate is maintained. The volume of product produced in a continual flow reactor ***is not*** a function of the size of the reactor volume.

The reaction chamber of Rosenberg is a typical batch reaction vessel, because it contains a "solid support" (for example, see page 4, lines 14-15; and page 17, lines 26-36 of Rosenberg's disclosure). Such solid supports are used in reactions that are characterized by including a first step in which a first reactant is attached to the solid support, a second step in which a second reactant is introduced to react with the first reactant bound to the solid support, and a final step in which the resulting product is released from the solid support. Thus, the volume of the product produced in the reactor is a function of the volume of the first reactant bound to the solid support. Rosenberg teaches that the coupling reaction is performed by cycling the amino acids through the reaction chamber where the first reactant is bound to the solid support as many times as required to complete desired coupling reaction (for example, see the second paragraph on page 24 of Rosenberg's disclosure). The cycling disclosed by Rosenberg is significantly different than the operation of a continuous flow reactor, where reactants are introduced into a reactor and a product exits the reactor in a continuous fashion as a function of a flow rate used to introduce the reactants into the reactor. Significantly, reactors configured to operate continuously generally include one or more internal

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volumes in which one or more reactants are mixed. No solid support is required to initiate the reaction. Thus, reactants and product can continually flow through the internal volumes of the reactor in a continuous process, rather than batch process. A preferred microreactor comprising a plurality of stacked plates and internal reaction volumes is described in the amended specification. The specification, both as amended and as originally filed, clearly describes operation of a reactor such that reactants are continuously introduced into a reactor, and a product is continuously collected from the reactor.

Significantly, the reaction time in a batch vessel is determined by the length of time the reactants are held within the reaction vessel. The reactor is ready for use again only after completely removing the reaction mixture and cleaning the reaction vessel to prepare it for reuse. Thus, a series of steps are required for performing one single reaction. Rosenberg describes a technically complicated delivery method (pressure/negative pressure, vacuum, etc.), as well a a cleaning cycle that occurs each time the reactor is used to process a batch.

In contrary, the reaction time in a reactor configured for continuous operation is determined by the interior volume of the reactor, the flow rate of the reactants to the reactor, and a length of time the flow rate is maintained. Thus, a volume of product significantly larger than the interior volume of the reactor can be produced, simply by maintaining a continuous flow rate through the reactor over a period of time required to achieve the desired production volume.

The use of a continuous flow reactor in place of a batch reactor enables numerous benefits to be achieved, benefits which do not appear to be recognized by the prior art. By using a spacer liquid to separate sequential reaction products (see FIGURE 4 of the specification as filed, with *S* representing a spacer liquid or solvent), it is possible to continuously perform a plurality of sequential syntheses using only a single reactor. While Rosenberg also implements a single reactor, the use of a continuous flow reactor in place of a batch reactor enables the following benefits to be obtained:

- *The amount of product is not determined by the inner volume of the reactor; the volume of the product can exceed or fall below the reactor volume, depending on flow rate and time.*
- *A relatively large library can be produced within a relatively short time using only a single reactor (because many of the cleaning steps required by Rosenberg are not required to use the reactor system of the present invention, total time to produce the desired library is significantly reduced).*

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- *At any one time there can be more than one different product moving through the entire system. Referring to FIGURE 4, as the last of product of A1B1 is being directed into a product collector, solvent used to flush the reactor is exiting the reactor, and reagents A1 and B2 are beginning to enter the reactor, to produce the product of A1B2. This feature leads to significantly shorter cycle times, as the cleaning cycle can be started during the reaction process, and not after the reaction process is completed.*
- *Downtime (i.e., the amount of time the reactor cannot be used to produce a product) required for cleaning is a function of the number of different chemical products being produced (i.e., A1B1, A1B2, etc, generally as indicated in FIGURE 4), not the number of different batches being produced. If Rosenberg's system is used to generate five batches of A1B1 and four batches of A1B2, then nine cleaning cycles will be required. Applicants' system can generate the same volume of A1B1 and A1B2 using only **two** cleaning cycles, meaning the reactor is available to be online producing product for a greater amount of time.*

The prior art simply does not teach or suggest any of the above-identified benefits. Thus, it appears that modifying Rosenberg's system to include a reactor configured for continuous processing requires an impermissible application of hindsight. Claim 15 has been similarly amended to recite a reactor configured for continuous operation. Furthermore, the language of Claim 15 has been amended to define the controller as manipulating the flow rates of the reactants to accommodate different reaction times for different reactions, the controller establishing a relatively higher flow rate for reactions requiring a relatively shorter reaction time, and the controller establishing a relatively slower flow rate for reactions requiring a relatively longer reaction time. Such a controller is not disclosed or suggested by Rosenberg. It is well recognized that the pending claims must be patentable for at least the same reasons as the claims upon which they depend. Accordingly, the rejection of Claims 1-6, 9, 11-16, and 18 under 35 U.S.C § 103(a) as being obvious over Rosenberg should be withdrawn.

Referring to Claims 6 and 18, the Examiner has admitted that Rosenberg does not specifically teach a detector located between the reaction chamber and the output valve. The Examiner has asserted that the incorporation of such a detector would have been obvious to one of ordinary skill in the art in order to control the process of product formation. Applicants respectfully disagree.

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Significantly, the automatic detector defined by applicants is configured to provide *an output signal to the system controller that is indicative of whether a spent solvent or a desired chemical product is flowing from the reaction module* (Claim 18 uses slightly different language, but parsing Claim 18 makes it clear that the detector must be capable of distinguishing a solvent from a product). If an artisan of ordinary skill was motivated to modify Rosenberg's synthesis system to control the process of product formation, there is no evidence that such an artisan would have been motivated to add a detector specifically configured to distinguish between a reaction product and a spent solvent. Rosenberg's apparatus is particularly well-suited to synthesize oligomers. The Examiner appears to argue that an artisan of ordinary skill would have been motivated to modify Rosenberg's apparatus to include a detector configured to detect oligomers. Such a detector is not equivalent to a detector configured to provide an output signal indicative of whether a spent solvent or a desired chemical product is flowing from the reaction module. Claims 6 and 18 are distinguishable over the cited art for this additional reason.

With respect to Claims 10 and 17, the Examiner admits that Rosenberg does not disclose a residence time chamber, and argues that it would have been obvious to one of ordinary skill in the art to incorporate residence time chambers such as those disclosed by Joslyn into Rosenberg's apparatus, to achieve an equivalent invention. As discussed in detail above, Rosenberg describes a batch reactor. Residence time chambers are uniquely suited for use with reactors configured for continuous processing, not batch processing. As discussed in detail above, it appears to require an impermissible application of hindsight to replace the batch reactor disclosed by Rosenberg with a continual process reactor as defined and recited in applicants' claims. Such an application of hindsight would appear to be similarly required to modify Rosenberg to incorporate a residence time chamber. For this additional reason, Claims 10 and 17 are distinguishable over the cited art.

Claim 13 has been amended to specifically define the outlet valve as comprising *a proportional valve configured to act as a throttle to enable a pressure along a reaction path to be selectively varied.* The specification as filed clearly refers such an embodiment (see page 15, second paragraph). Rosenberg discloses a pressure source (such as an argon cylinder) being included to enable pressure conditions to be varied. However, the pressurized gas supply disclosed by Rosenberg is not equivalent to a proportional valve being disposed in between a reactor and an automated product collector. It appears such a modification would require an impermissible use of hindsight. Claim 13 is therefore distinguishable over the cited art for this additional reason.

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Patentability of Newly Added Claims

Newly added Claim 28 is based on Claim 1 as originally filed, with the incorporation of the additional elements of the detector of Claim 6 and a controller configured to analyze the output signal provided by the detector to selectively actuate the output valve to either *couple the reaction module in fluid communication with the automated product collector* or *to couple the reaction module in fluid communication with the spent solvent reservoir*.

As discussed in detail above, a detector configured to distinguish between a solvent and a product does not appear to be reasonably disclosed by the cited art, nor does the cited art appear to support the conclusion that it would have been obvious to modify Rosenberg's system to include such an element. Even if, as the Examiner suggests, one of ordinary skill in the art would have been motivated to modify Rosenberg's apparatus to include some sort of detector, there is no evidence that such an artisan would have selected a detector configured to distinguish between a solvent and a product, or to configure the controller to selectively actuate the output valve as noted above. It appears such a modification would require an impermissible use of hindsight. Claim 28 is therefore distinguishable over the cited art.

Accordingly, all of the claims now submitted define patentable subject matter that is neither anticipated nor obvious in view of the prior art cited. The Examiner is thus requested to issue the present patent in view of the amendments and the remarks submitted above. If there are any questions that might be addressed by a telephone interview, the Examiner is invited to telephone the undersigned attorney, at the number listed below.

Respectfully submitted,

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MCK:elm

MAILING CERTIFICATE

I hereby certify that this correspondence is being deposited with the U.S. Postal Service in a sealed envelope as first class mail with postage thereon fully prepaid addressed to: Commissioner for Patents, Alexandria, VA 22313-1450, on April 4, 2006.

Date: April 4, 2006

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